Research Highlight

Aortic valve calcium load before TAVI: Is it important?

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Cardiac surgeons were trained for decades to avoid paravalvular leakage as a major complication after aortic valve replacement. In contrast, with the widespread use of transcatheter aortic valve implantation techniques, paravalvular leaks are now considered as an acceptable outcome without serious consequences by some investigators. This might be true for trivial or mild paravalvular incompetence in patients within their last decade of life. However, with a more liberal TAVI indication, i.e. TAVI expansion to operable patients, even mild paravalvular leaks might be a matter of concern. For the first time, on the basis of a prospective, multicenter, randomized clinical trial, even mild paravalvular leaks have been associated with an increased long-term mortality (1). In addition, a recent study from the German transcatheter aortic valve registry has revealed that patients with paravalvular leaks are not just sicker in general, but are prone to a considerably higher in-hospital mortality (2). Thus, Aortic Valve Calcium Scoring (AVCS) pre-TAVI might be important with regard to outcome and paravalvular leaks.

A recent study at the Heart Center Leipzig demonstrated a significant association between native aortic valve calcification and paravalvular leak in 120 patients [odds ratio (OR; per AVCS of 1,000), 11.38; 95% confidence interval (CI), 2.33-55.53; P=0.001, (3)]. Echocardiography (ECG)-gated cardiac computed tomography quantified the amount of calcification of the aortic valve leaflets using a scoring system analogous to the Agatston calcium scoring of coronary arteries [Aortic Valve Calcium Scoring (AVCS), *Figure 1*]. Paravalvular leaks were assessed and quantified intra-operatively by transoesophageal echocardiography (TEE) and root angiography. All valves were implanted successfully. The mean AVCS in patients without paravalvular leaks (n=66) was 2704±1510; with mild paravalvular leaks (n=31) was 3804±2739 (P=0.05); and with moderate paravalvular leaks (n=4) was 7387±1044 (P=0.002) (*Table 1* and *Figure 2*). Consistent with this study, two further studies documented comparable results using the CoreValve ReValving system (4,5). Wood *et al*. (6) in contrast, did not find an association between paravalvular leaks and the degree of calcification, which was probably a result of the small study population.

When analysing the localization of paravalvular leaks based on TEE, there was also a significant relation to the AVCS in each separate cusp or commissure (*Table 2*). A significant association was found for the right and left coronary cusp, and for the right-left and left-non-coronary commissure. This association, however, failed to reach statistical significance for the non-right-coronary commissure and the non-coronary cusp. One possible reason for this might be the intrinsic weakness and elasticity of the annulus in this area, leading to an anatomic predisposition to paravalvular leaks (7).

There is well-accepted agreement, that valve calcification is a surrogate marker for the biological age and general morbidity of an individual patient. Temporary haemodialysis as well as ventilation time were both associated with a significantly higher AVCS (*Table 3*). More frequently increased AVCS values were observed in those with impaired respiratory function and renal disease, thus, suggesting that these patients are at a higher risk for post-procedural secondary complications and a longer in-hospital stay. Based on our experience, however, the AVCS was not a predictor of 30-day mortality, major cardiac events and stroke.

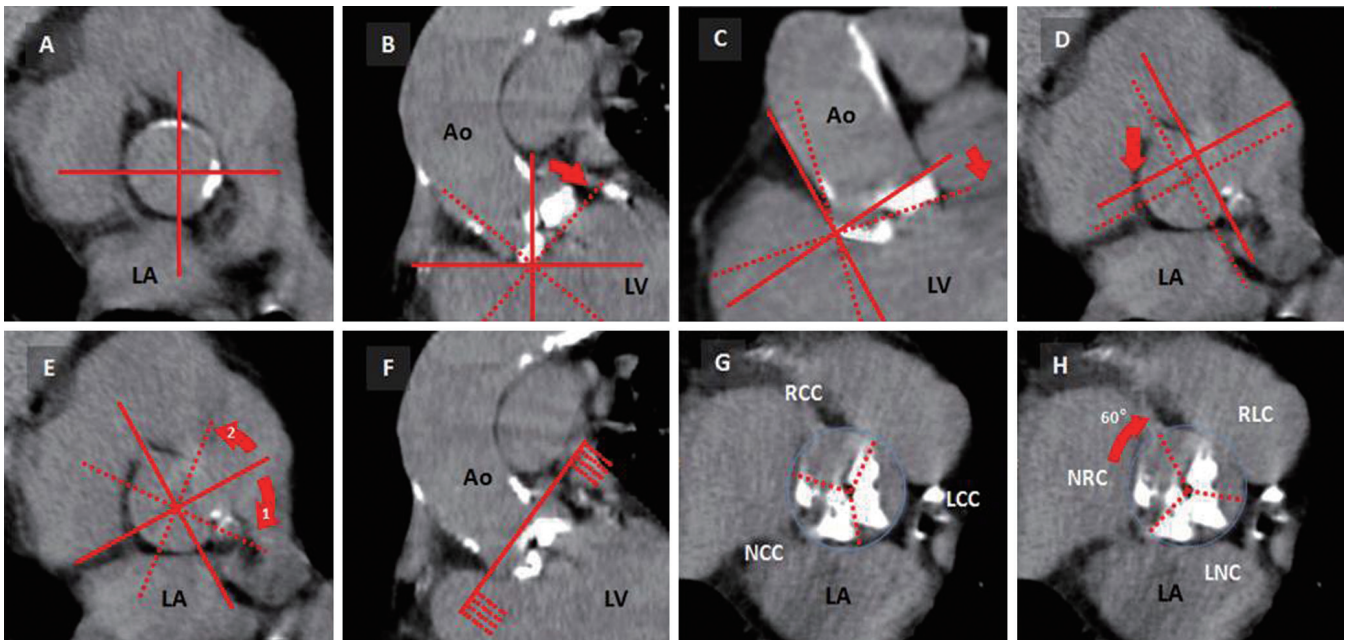


Figure 1 Aortic Valve Calcium Scoring (AVCS): Step by step. A: Place the crosshair on the aortic sinus in a transverse section. Switch to coronal view. B: Move the crosshair centre to the lowest part of the basal attachment of the NCL and rotate the crosshair until one plane reaches the corresponding part of the LCL. C: Switch to the sagittal view. Adapt the plane to the lowest part of the basal RCL attachment. Control the plane position by scrolling through the image stack. D: Switch to oblique transverse view to display the entire aortic annulus. Place the crosshair in the centre of the aortic annulus. E: Rotate the crosshair until the coronary ostia of LCA (1) and RCA (2) appear in the coronal or sagittal view. F: Select the entire aortic valve. Create a batch that reaches from the sinotubular junction to the basal attachments of the cusps. G: Create a batch for every cusp. Measure the AVCS for the entire valve and each separate cusp. H: Repeat step G for every commissure by rotating the selected area 60° clockwise. Measure the AVCS for each separate commissure

Table 1 Preoperative transesophageal echocardiography results and mean Aortic Valve Calcium Score's (AVCS) for the aortic valve, cusps and commissures depending on the presence of a paravalvular leak

AVCS	No paravalvular leak*	Paravalvular leak*	P-value
Aortic valve	2694±1528	4153±479	0.006
Right coronary cusp	811±542	1189±882	0.025
Left coronary cusp	919±644	1669±1514	0.001
Non-coronary cusp	1013±671	1281±750	0.053
Right-left-coronary commissure	782±554	1295±1071	0.010
Left-non-coronary commissure	1049±656	1589±1104	0.012
Non-right-coronary commissure	918±560	1258±941	0.110

Aortic Valve Calcium Score's (AVCS) for the aortic valve, cusps and commissures depending on the presence of a paravalvular leak. *: confirmed by intraoperative transesophageal echocardiography (TEE) and root angiography

In contrast, in a previously published study (8) the degree of aortic valve calcification (calcium mass-score) was a significant predictor for 30-day MACE and for 1-year mortality. Patients with severe periprocedural complications (death, acute myocardial infarction and stroke) revealed significant more aortic valve calcium than patients without any complications. By selecting a calcium mass-score threshold of 750 the authors were able to identify more than 70% of patients who suffered subsequently from MACE or died within the first year. They concluded that such a parameter had enormous value in order to better select and risk-stratify candidates for TAVI.

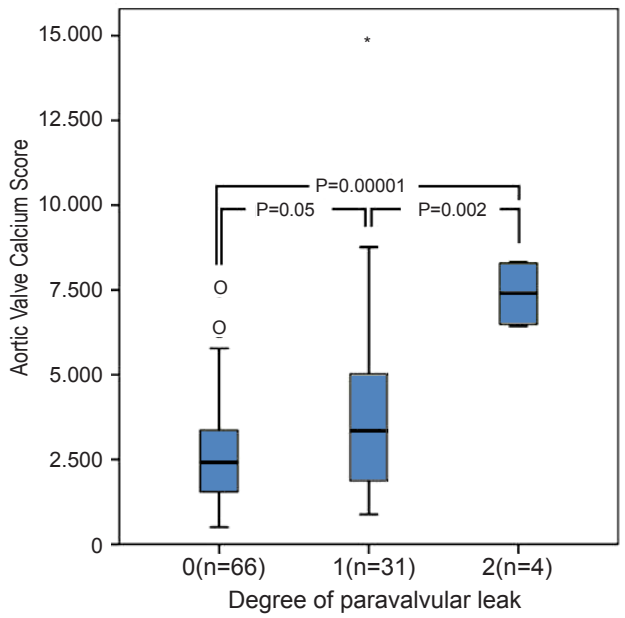


Figure 2 Mean AVCS for the entire aortic valve depending on the degree of a paravalvular leak. Significantly higher mean AVCS scores were found in patients with mild (1) and moderate (2) paravalvular leaks

Table 2 Association of Aortic Valve Calcium Score (AVCS), localization and degree of paravalvular leaks

Impact of aortic valve calcification on paravalvular leaks				
		Localization of paravalvular leak (TEE)		
		R	L	N
Calcium Score cusp (CT)	R	5.64 P=0.018	1.84 P=0.17	1.03 P=0.87
	L	1.94 P=0.16	5.43 P=0.020	1.61 P=0.20
	N	1.85 P=0.17	3.59 P=0.058	1.35 P=0.56
		RL	LN	NR
commissure	RL	4.88 P=0.027	2.70 P=0.10	1.02 P=0.90
	LN	1.66 P=0.20	5.03 P=0.020	1.24 P=0.63
	NR	1.27 P=0.61	2.25 P=0.13	1.37 P=0.24

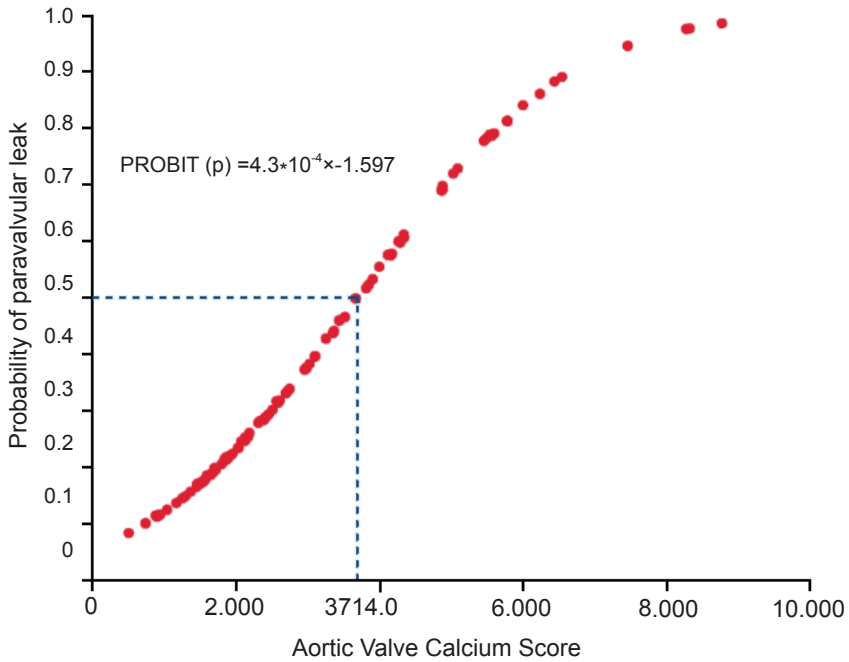
Data are presented as odds ratio per AVCS of 1000 and corresponding P-values. *confirmed by intraoperative transesophageal echocardiography. Abbreviations: R, right coronary; L, left coronary; N, non-coronary; RL, right-left coronary; LN, left-non coronary; NR, non-right coronary

Table 3 Impact of aortic valve calcification on outcome.

	CI	*OR*	p-value
Paravalvular leak*	[2.33;55.53]	11.38	0.001
Major cardiac event	[0.68;1.25]	0.92	0.57
Stroke	[0.41;1.96]	0.90	0.79
New pacemaker-implantation	[0.85;1.89]	1.27	0.26
Temporary hemodialysis	[0.96;14.53]	3.73	0.049
Median ventilation time ≥ 60 h	[1.73;36.56]	7.94	0.005
Reintubation	[0.86;9.82]	2.90	0.089
30-day mortality	[0.84;1.32]	1.05	0.68

Data are presented as odds ratio per AVCS of 1,000, corresponding P-values and confidence intervalls (CI). *confirmed by postoperative transthoracic echocardiography before discharge

Cardiac computed tomography (CT) is the gold standard imaging technique for assessing aortic valve calcification. Although, the cardiac CT-based AVCS has not been not cross-validated with the intraoperative transesophageal echocardiography (TEE), TEE assessment may add further information to better understand the morphology of the native calcified valve. A recent paper by Colli *et al.* (9) has examined the usefulness of an echocardiographic calcification score (ECS) to predict outcomes in 103 transapical TAVI patients. The ECS, as well as the aortic commissure calcification score alone, were predictive for the development of post-TAVI aortic regurgitation. The ECS was associated with the presence of moderate paravalvular aortic regurgitation (odds ratio 8.5; 95% confidence intervall, 1.2-58.9; P=0.0001) and overall moderate aortic regurgitation (odds ratio 3.6, 95% confidence intervall, 1.2-10.4; P=0.0006). The TEE gave detailed anatomic information of the calcification patterns of the aortic valve. The echocardiographic



AVCS Cut-off Score (n = 120)	Probability of a paravalvular leak
732.6	0.10
2145.3	0.25
3714.0	0.50
5282.6	0.75
6695.3	0.90

Figure 3 Probability of a paravalvular leak depending on the aortic valve calcium score

calcification score (ECS) may be used to identify patients at high risk for the development of post-TAVI AR and may therefore support decision making in the future. The main drawback of the study from Colli *et al.* (9) is the retrospective nature. Prospective randomized studies will be necessary to conclusively answer the question whether preoperative AVCS should be mandatory and helpful to predict AR after TAVI.

On the other hand, a more calcified aortic root might offer superior grip and better seating in the native annulus during deployment. In a study by van Miegham *et al.* (10) patients with valve dislodgment had significantly less aortic root calcification using the Medtronic CoreValve™ system [median Agatston score 1,951 AU (IQR, 799-3,103) *vs.* 3,289 AU (IQR 2,097-4,481), P=0.016]. The incidence of valve dislodgment was three times higher when the Agatston calcification score was <2,359 AU by multi-slice computed tomography. Thus, in patients with a low AVCS the impact of aortic root calcium score on valve dislodgment seems robust and warrants further awareness among surgeons.

In summary, the AVCS identifies patients at risk for a relevant paravalvular leak. The AVCS prior to TA-AVI might serve as an additional tool for surgeons to reconsider the TAVI indication and valve size to reduce the risk of paravalvular leaks (*Figure 3*). Clinically, we especially consider patients with a borderline risk score and a high calcium burden as 'non-TAVI candidates' (3). In self-expanding transcatheter heart valves which don't have the same radial forces as balloon-expandable valves, it may even play a major role, and even more impact on the postoperative result in terms of the persistence of paravalvular leaks and residual stenosis. If we can predict somehow whether these patients will have TAVI regurgitation or not, and this is one way to do it, it will in the future help us to define the best valve for a given patient and the best procedure.

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